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CASE REPORT

Superselective docetaxel—nedaplatin combined infusion concurrent with radiation therapy in advanced oral cancers

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KEYWORDS

Superselective intra-arterial chemotherapy concurrent with radiotherapy;
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Summary Cisplatin-based superselective intra-arterial chemotherapy concurrent with radiotherapy (SIART) has been reported to be effective in advanced head and neck carcinomas (HNC). However, the ideal regimen has not been established. We combined nedaplatin (CDGP) with docetaxel (DOC) as a new combination in SIART for treatment of advanced oral squamous cell carcinomas (OSCC). Two patients with stage IV advanced OSCC were treated and complete response (CR) were attained, although a residual metastatic lymph node remained in one case. Thirteen and 10 months post-treatment, no recurrence or metastatic spread was observed. This result indicated that CDGP and DOC combination in SIART is effective in advanced OSCC treatment.

Introduction

Chemotherapy, radiotherapy and surgery are the main treatment of the head and neck carcinomas (HNC). Although combination of surgery and radiotherapy is considered to be a standard treatment,[1,2] outcome of HNC therapy is not satisfactory in term of survival rates particularly in patients with stages III and IV advanced neoplasm.[3,4] Furthermore, in weighing the cost-benefit of treatment, organ preservation in treatment of advanced HNC is another important consideration for quality of life (QOL).[5]

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In order to overcome these problems, superselective intra-arterial chemotherapy concurrent with radiotherapy (SIART) has become popular in advanced HNC treatment.[6,7] Cisplatin (CDDP) together with docetaxel (DOC) have been reported to be the ideal chemotherapeutic agents.[8–12] Recently, nedaplatin (CDGP), an analogue of cisplatin with less toxicity, was reported to be effective for HNC treatment.[13,14]

The purpose of this report is to describe the efficacy of two agents, DOC and CDGP as a new combination in SIART, used in the treatment of two cases of T4 advanced oral squamous cell carcinomas (OSCC), where complete response (CR) was obtained in the primary region with no consequent surgical procedure.

Report of cases

Treatment procedure

After the assessment of the tumor invasion extent by computed tomography (CT) and magnetic resonance imaging (MRI), selection of the feeding arteries of the tumor by CT angiography (CTA) and digital subtraction angiography (DSA) via femoral artery was conducted. A total of 66 Gy of irradiation was initiated for a period of seven weeks concurrent with three courses of DOC (60 mg/body) and CDGP (80 mg/m^2) combination of chemotherapeutic agent infusion. After final evaluation by radiographic examination and incisional biopsy

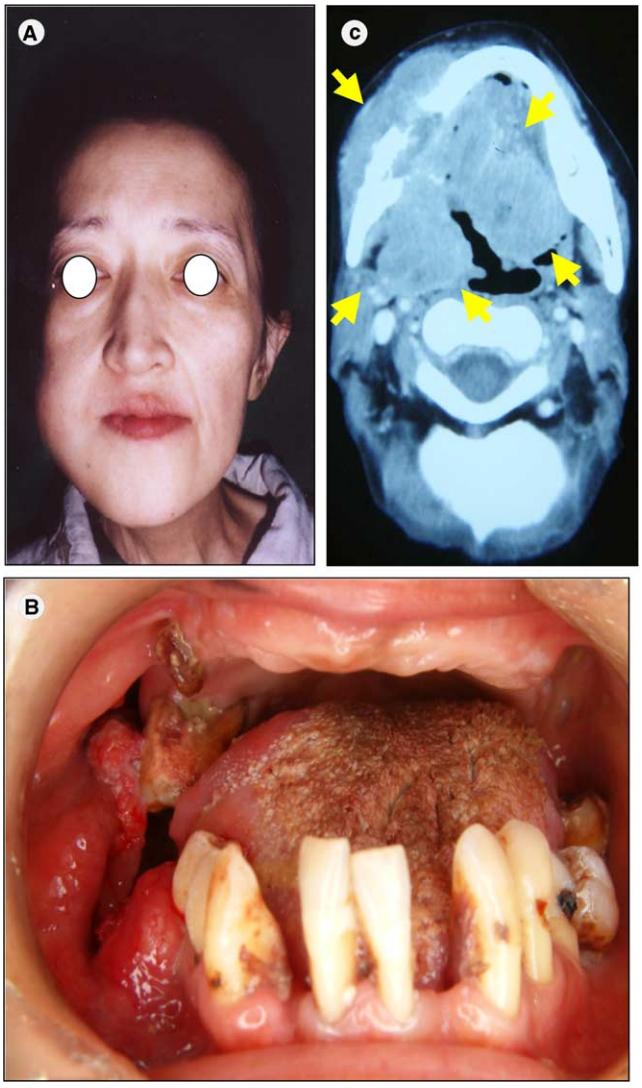

Figure 1 Pre-treatment extra (A) and intra-oral photograph (B). (C) Computed tomography revealed the extent of the tumor invasion (arrows).

the patients were discharged as no residual tumor was found in the primary region.

Case 1

A 45-year-old woman diagnosed with advanced OSCC was referred to our department. The patient facial countenance was asymmetrical as the result of right facial induration by palpable tumor but no skin invasion was observed. Metastatic lymph nodes (mLN) were identified bilaterally in the superior-internal-jugular region. Fig. 1 shows the photographs and enhanced-CT of the patient. A T4N2c poorly differentiated OSCC of the right gingival of the mandible was diagnosed after incisional biopsy was performed. SIART was opted for the treatment where selection of the feeding arteries (facial, lingual, infra-alveolar and ascending pharyngeal) was determined by CTA and DSA (Fig. 2A). After three courses of the combined treatment, CR was obtained in the primary site although a reduced size mLN remained at the right superior-internal-jugular region. Radical neck dissection was planned but the patient declined to undergo operation. The patient was discharged four months after admission and observation is carried out with chemotherapeutic medication prescribed. Thirteen months post-treatment, no primary recurrence or progression of the residual mLN was observed (Fig. 2B and C).

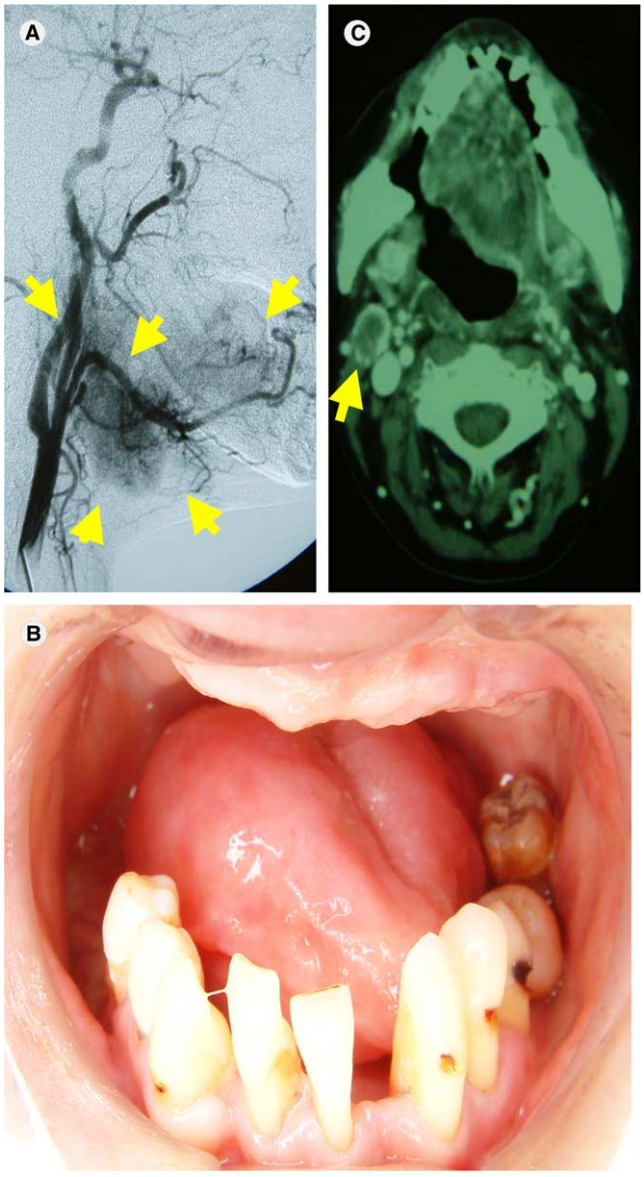

Figure 2 (A) DSA of the feeding arteries. Arrows indicate the staining extent of the tumor. (B) Clinical view 13 months post-treatment, and (C) computed tomography where residual metastatic lymph node is observed (arrow).

Case 2

A 47-year-old woman with swelling of the submental region and a swollen tongue was referred to our department (Fig. 3). A T4N2a well-differentiated OSCC of the tongue was diagnosed by radiography and incisional biopsy and the patient opted for SIART. The feeding arteries were just the same

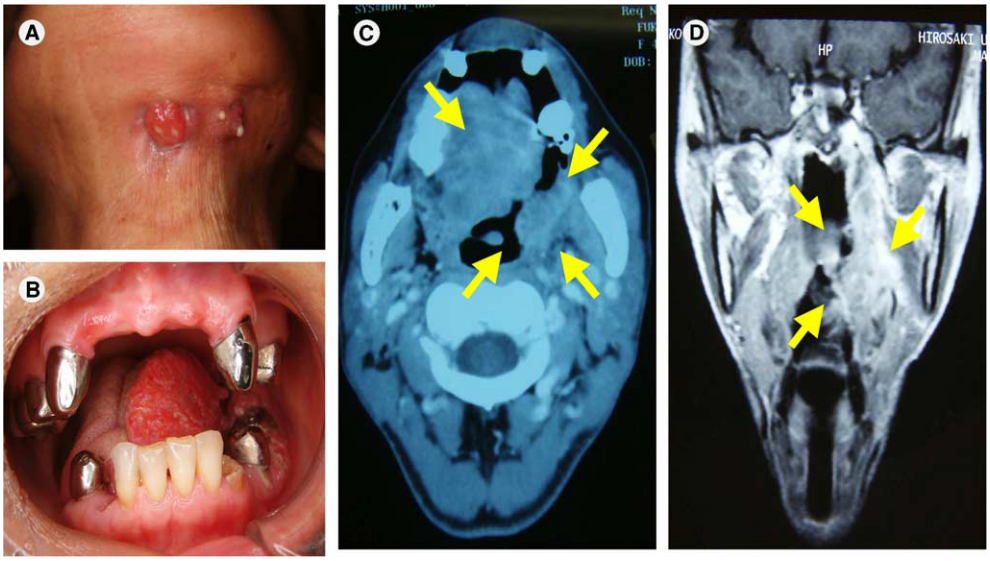

Figure 3 (A) Swelling at submental region. (B) Pre-treatment intra-oral photograph. (C) Pre-treatment computed tomography and magnetic resonance imaging (D). Arrows indicate the tumor invasion extent.

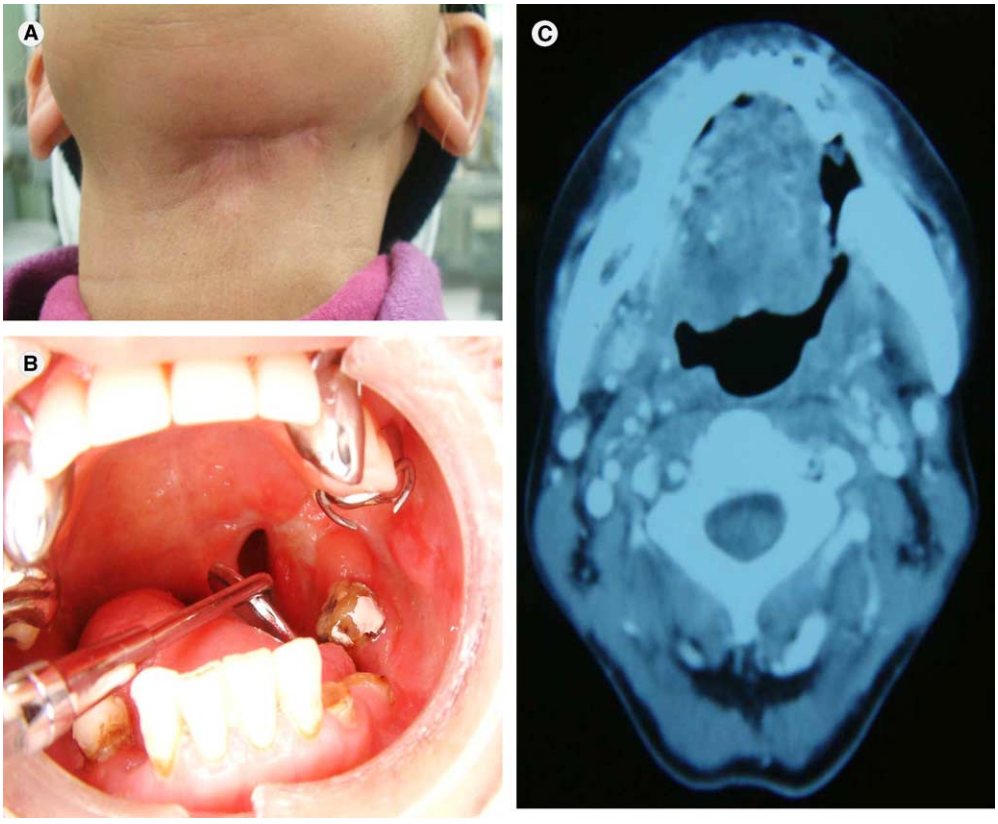

Figure 4 Ten months post-treatment. Extra-oral (A) and intra-oral photograph (B). (C) No tumor observed in computed tomography.

as in case 1. After three courses of the combined therapies, no residual tumor was observed. There was no evidence of recurrence or metastatic spread either at the primary site or in the neck 10 months post-treatment (Fig. 4).

Discussion

For the last decade, SIART has been extensively conducted and has become a common and effective therapy in advanced HNC.[6,7,15,16] Although various chemotherapeutic agents have been tried, there is still no consistently dependable regimen available. Numerous CDDP based-regimens have been cited as effective in HNC treatment,[8,9,17,18] although severe nephrotoxicity, mucositis, nausea and anorexia develop in some cases and treatment has to be suspended.

CDGP, an analogue of CDDP, was developed recently and reported to be as effective or superior to CDDP in treatment of HNC.[13,14] The pH of CDGP was 7.0 and did not caused angialgia during the infusion and no neutralizer was needed. Renal toxicity is rare where post-treatment hydration is limited. Although more severe myelotoxicity particularly thrombocytopenia was observed, CDGP has fewer gastrointestinal symptoms and treatment suspension due to the side effects was not reported.[14]

In this paper, two cases of T4 advanced OSCC are reported who were treated by SIART using a combination of CDGP and DOC. DOC, a taxane, has significant response reported in HNC,[10] and the mechanism of action against tumor cells was totally different from CDDP. In both cases CR was obtained in the primary region, although residual mLN remained in case 1. Besides clinical examination, CT and MRI post-treatment were conducted to assess the treatment effect. Incisional biopsy was taken and no viable cells were identified.

Advanced OSCC tend to have more than one feeding artery and trans-femoral artery approach has the advantage of administrating the chemotherapeutic agents to multiple arteries feeding the tumor, as compared to conventional SIART. However, it is hard to obtain a good response rate in mLN because the feeding arteries are complicated and difficult to locate. Therefore, neck dissection is considered to be appropriate for cases where mLN were confirmed.[19]

The side effects of treatment in the two cases included a grade II reverse hemicranial alopecia, a grade III neutropenia, where reversion of the neutrophil count was achieved after injection of G-CSF, and a grade III mucositis requiring no interruption of irradiation. No thrombocytopenia was observed, although mild to severe thrombocytopenia has been reported in cases where CDGP was administrated independently.[14] Both patients continued oral diet during the treatment period with good pain-control gained by using analgesic of NSAID and morphine.

In conclusion, the regimen of DOC and CDGP combination of chemotherapeutic agents used in SIART showed a good response where CR was obtained in treatment of advanced OSCC with manageable toxicities. No relapse of tumors and no progression or spreading of mLN was evident in the two cases 13 and 10 months post-treatment. At least four weeks of interval period was needed between the SIA chemotherapies due to the development of neutropenia from DOC and CDGP, which prolonged the treatment period for more than three months.

References

1. Vikram B, Strong EW, Shah J, Spiro RH. Elective postoperative radiation therapy in stages III and IV epidermoid carcinoma of the head and neck. *Am J Surg* 1980;**140**(4): 580—4.
2. Brizel DM, Albers ME, Fisher SR, et al. Hyperfractionated irradiation with or without concurrent chemotherapy for locally advanced head and neck cancer. *N Engl J Med* 1998;**338**(25):1798—804.
3. Cachin Y, Eschwege F. Combination of radiotherapy and surgery in the treatment of head and neck cancers. *Cancer Treat Rev* 1975;**2**(3):177—91.
4. Dimery IW, Wendt CD, Kramer AM, Byers RM, Hong WK. The role of induction chemotherapy for organ preservation in laryngeal carcinoma. *Cancer Treat Res* 1990;**52**: 209—22.
5. Funk GF, Karnell LH, Christensen AJ, Moran PJ, Ricks J. Comprehensive head and neck oncology health status assessment. *Head Neck* 2003;**25**(7):561—75.
6. Lee YY, Wallace S, Dimery I, Goepfert H. Intraarterial chemotherapy of head and neck tumors. *AJNR Am J Neuroradiol* 1986;**7**(2):343—8.
7. Hollmann K, Mailath G, Rasse M, Kuhlbock J, Stadler B. Regional chemotherapy of inoperable maxillofacial tumours combined with radiotherapy. Long-term results. *J Craniomaxillofac Surg* 1990;**18**(2):88—90.
8. Robbins KT, Vicario D, Seagren S, et al. A targeted supradose cisplatin chemoradiation protocol for advanced head and neck cancer. *Am J Surg* 1994;**168**(5): 419—22.
9. Kerber CW, Wong WH, Howell SB, Hanchett K, Robbins KT. An organ-preserving selective arterial chemotherapy strategy for head and neck cancer. *AJNR Am J Neuroradiol* 1998;**19**(5):935—41.
10. Dreyfuss AI, Clark JR, Norris CM, et al. Docetaxel: an active drug for squamous cell carcinoma of the head and neck. *J Clin Oncol* 1996;**14**(5):1672—8.
11. Hanauske AR, Schilling T, Heinrich B, et al. Clinical phase I study of paclitaxel followed by cisplatin in advanced head

and neck squamous cell carcinoma. *Semin Oncol* 1995;**22**(6 Suppl 14):35—9.
12. Pronk LC, Schellens JH, Planting AS, et al. Phase I and pharmacologic study of docetaxel and cisplatin in patients with advanced solid tumors. *J Clin Oncol* 1997;**15**(3): 1071—9.
13. Alberts DS, Fanta PT, Running KL, et al. In vitro phase II comparison of the cytotoxicity of a novel platinum analog, nedaplatin (254-S), with that of cisplatin and carboplatin against fresh, human ovarian cancers. *Cancer Chemother Pharmacol* 1997;**39**(6):493—7.
14. Ita M, Okafuji M, Fukuda K, Mitsuoka K, Hanakita T, Hayatsu Y. Concurrent chemoradiotherapy with new platinum compound nedaplatin in oral cancer. *Oral Oncol* 2003;**39**(2): 144—9.
15. Kovacs AF. Intra-arterial induction high-dose chemotherapy with cisplatin for oral and oropharyngeal cancer: long-term results. *Br J Cancer* 2004;**90**(7):1323—8.
16. Robbins KT, Kumar P, Regine WF, et al. Efficacy of targeted supradose cisplatin and concomitant radiation therapy for advanced head and neck cancer: the Memphis experience. *Int J Radiat Oncol Biol Phys* 1997;**38**(2):263—71.
17. Vokes EE, Ratain MJ, Mick R, et al. Cisplatin, fluorouracil, and leucovorin augmented by interferon alfa-2b in head and neck cancer: a clinical and pharmacologic analysis. *J Clin Oncol* 1993;**11**(2):360—8.
18. Rooney M, Kish J, Jacobs J, et al. Improved complete response rate and survival in advanced head and neck cancer after three-course induction therapy with 120-hour 5-FU infusion and cisplatin. *Cancer* 1985;**55**(5):1123—8.
19. Robbins KT, Wong FS, Kumar P, et al. Efficacy of targeted chemoradiation and planned selective neck dissection to control bulky nodal disease in advanced head and neck cancer. *Arch Otolaryngol Head Neck Surg* 1999;**125**(6): 670—5.